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LETTER

Letter to the Editor Regarding "Colchicine Against SARS-CoV-2 Infection: What is the Evidence?"

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To the editor:

We read with interest the narrative review by Drosos et al. concerning colchicine as a potential therapeutic agent against SARS-CoV-2, its mode of action, its pleiotropic effects on neutrophils, its inhibition of the inflammasome, and its anti-viral activity [1]. It was concluded that there is ample evidence that colchicine is effective, safe, and easy to use and therefore a promising drug for the treatment of severe COVID-19 [1]. The review is attractive but raises concerns that need to be discussed.

We disagree that colchicine is an effective therapeutic option for COVID-19 [1]. There are a number of conflicting results. Several studies have shown that colchicine does not prevent infection with SARS-CoV-2 [2], nor can morbidity or mortality of SARS-CoV-2 infections be improved by continuous use of colchicine [3]. In a retrospective study of 14,520 patients tested for SARS-CoV-2, seven of those who took colchicine regularly prior to PCR testing for SARS-CoV-2 ($n = 71$) were SARS-CoV-2 positive (0.53%) and 64 were SARS-CoV-2 negative (0.48%) [2]. The absence of a significant difference ($p = 0.817$) speaks against an effect in the prevention of SARS-CoV-2 infections [2]. A meta-analysis of four randomized control trials (RCTs) on the effect of colchicine in COVID-19 patients showed no significant effect of colchicine on mortality [3]. A meta-analysis of ten RCTs using the random-effect model to estimate the pooled odds ratio (OR) of mortality and the confidence interval (CI), showed no significant difference in the odds for mortality (pooled OR = 0.76; 95% CI 0.53–1.07) [4]. According to the RECOVERY trial with 11,340 COVID-19 patients, colchicine showed no evidence of clinical benefits in terms of mortality, hospitalization, or disease progression [5]. The authors of this study concluded that colchicine should not be used in clinical practice or used in clinical research without conducting additional large RCTs [5].

We also disagree that colchicine is safe in COVID-19 patients [1]. Although no systematic studies on the safety profile of colchicine have been conducted, there are several case reports and case studies showing that colchicine has not only beneficial but also undesirable effects. A 64-year-old male taking colchicine for gouty arthritis developed quadruparesis with proximal predominance, accompanied by severely elevated muscle enzymes and a myogenic electromyography (EMG) [6]. Discontinuation of the drug resulted in a speedy recovery [6]. A

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systematic review of 36 observational studies showed that there is evidence that colchicine is associated with an increased risk of infections, particularly pneumonia, urinary tract infections, and *Helicobacter pylori* and *Clostridium difficile* infections [7].

A third point to note is that interactions between colchicine and several other drugs have been reported. In particular, patients receiving statins or fibrates in addition to colchicine may develop myopathy. In a safety meta-analysis of four studies involving 11,594 patients with cardiovascular disease, serious drug–drug interactions were identified not only between colchicine and lipid-lowering drugs, but also between colchicine and carvedilol, non-dihydropyridine calcium channel blockers (verapamil and diltiazem), and amiodarone, digoxin, and quinidine [8].

Overall, the interesting review has some limitations which call its results and its interpretations into question. More RCTs are needed before evaluating the efficacy of colchicine in COVID-19 on morbidity, number and duration of hospitalizations, and mortality. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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